



BLOCK DRUG COMPANY, INC.

257 Cornelison Avenue Jersey City, N.J. 07302-3198
Telephone (201) 434-3000

3415 '00 NOV -7 P2:53

Next Day Air
Return Receipt Requested

November 6, 2000

Food and Drug Administration
Dockets Management Branch (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, MD 20857

RE: Docket 77N-0094

Request for Feedback Meeting to Amend the Tentative Final Monograph for Internal Analgesic, Antipyretic and Antirheumatic Drug Products for Over-the-Counter Use- Reclassification of Salicylamide as a Category 1 Analgesic Adjuvant

Dear Sir/Madam:

Block Drug Company, Inc. (Block) has been marketing its BC line of internal analgesics products containing aspirin, salicylamide and caffeine for over 30 years. Throughout the rulemaking process, Block Drug Company has submitted comments and data, through the feedback mechanism, to support the role of salicylamide as a safe and effective therapeutic adjuvant.

In May, 1989 representatives from Block met with the Agency to discuss the results of a pharmacokinetic study and obtain feedback on the protocol design of a more definitive pharmacokinetic and clinical study required to reclassify salicylamide to Category I. FDA recommended that caffeine be removed from the product because it contained two category III adjuvants and was unlikely to be reclassified to Category I. Although the TFM indicated that new data was to be submitted by 11/16/89, Block was assured that this date would not apply to us, since the feedback procedure had been initiated. Throughout the next few years, there was ongoing dialogue and communication with the Agency to finalize the protocols and conduct the appropriate studies necessary to demonstrate the analgesic adjuvancy of salicylamide in combination with aspirin.

77N-0094

C237

On July 29, 1994, Block submitted the results of two clinical studies using the oral surgery model. One of the studies also had a pharmacokinetic component. The results demonstrated that 195 mg of salicylamide was an effective analgesic adjuvant when co-administered with 650 mg of aspirin. It was also shown that the combination was both safe and effective as an OTC internal analgesic product when used as directed. However, we have not yet received feedback on this submission from the Agency.

In mid-1995, following review of the data submitted by five manufacturers on the analgesic adjuvancy of caffeine, FDA informed industry, via feedback letters, that caffeine would be a category I analgesic adjuvant in combination with aspirin or aspirin and acetaminophen.

Recently Block completed a study entitled "Aspirin Pharmacokinetics in Drug Combinations" (BD99-003). This study provides additional information on the role of salicylamide as an analgesic adjuvant in the presence of Aspirin and Caffeine.

The purpose of this letter is to request a meeting, under the feedback mechanism, to discuss the results from our recently completed pharmacokinetic study (BD99-003) and the pharmacokinetic profile of salicylamide developed throughout the rulemaking process. We would also like to discuss the results of the submission of July 1994. We believe that this meeting will help FDA finalize its deliberations on the reclassification of salicylamide as an analgesic adjuvant.

Objectives

1. To obtain the Agency's feedback on the adequacy of the data to reclassify salicylamide as an analgesic adjuvant from Category III to I with aspirin alone.
2. To obtain the Agency's advice and guidance with respect to the details of the proposed clinical study to demonstrate the contribution of Salicylamide as an adjuvant when combined with Aspirin and Caffeine.
3. To discuss interim marketing protection for our current BC formulation should the final monograph issue while we are conducting additional clinical studies.

Proposed Agenda

Introduction

Review of all pharmacokinetic data

Results of clinical studies submitted to the monograph

Proposed outline of clinical protocol to support the adjuvant status of salicylamide in combination with caffeine and salicylamide

Conclusion and discussion

Questions/Issues to be Addressed

- 1) Pursuant to the TFM requirements to reclassify salicylamide to a Category I adjuvant, are the pharmacokinetic and clinical studies, which were designed to demonstrate the adjuvancy of salicylamide in the presence of aspirin, sufficient to obtain Category I status for this combination?
- 2) Is the enclosed proposed clinical study design (ASA + CAF + SAL vs ASA + CAF vs. PBO) adequate to satisfy FDA requirements for reclassification of salicylamide in the presence of aspirin and caffeine?
- 3) If the Internal Analgesic Monograph finalizes before we complete our clinical program to demonstrate the adjuvancy of salicylamide in combination with aspirin and caffeine, will FDA grant us permission to continue marketing BC powder while the data review and proposed clinical studies are in progress?

Block Attendees

Frederick Curro, V.P./Director Corporate Clinical and Medical Affairs
Richard K. Bourne, Ph.D., V. P. Regulatory Affairs
Iris H. Shelton, Director Regulatory Affairs
Linda Dangler-Gendreau, Associate Director Clinical Research
Arlene Swern, Associate Director Biostatistics and Data Management
Consultant

We suggest that the following Agency personnel be present from the Division of OTC Drug Products as well as a reviewer from Biopharmaceutics.

Charles Ganley, M.D., Director
Linda Katz, M.D., Deputy Director,
Debbie Lumpkins, Team Leader
Rosemarie Neuner, M.D., Medical Officer
Thomas Parmelee, Pharm. D., Project Manager

We would be available to meet at anytime during the week of January 25, 2000 and will provide a briefing document at least 4 weeks prior to the subject meeting.

Should you have any questions or require additional information, please contact the undersigned at (201) 434-3000 ext. 1150.

Sincerely,



Iris H. Shelton

Desk Copy:
Dr. T. Parmelee

BLOCK DRUG COMPANY, INC.
257 CORNELISON AVENUE
JERSEY CITY, NEW JERSEY 07302
(201) 434-3000

PROTOCOL SUMMARY

Study # 00-xxx

Title: An Acute Analgesic Efficacy Study of the Co-Administration of Salicylamide 195 mg and Caffeine 65 mg with Aspirin 650 mg in Patients Following Oral Surgery

Objective: The objective of this study is to compare the analgesic effectiveness of the co-administration of Salicylamide and Caffeine with Aspirin compared to placebo.

A secondary objective is to compare the relative effectiveness of the co-administration of Salicylamide and Caffeine with Aspirin to the effectiveness of administering Caffeine with Aspirin.

Test Products: Active 1 (Aspirin 650 mg, Salicylamide 195 mg, Caffeine 65 mg)
Active 2 (Aspirin 650 mg, Caffeine 65 mg)
Placebo

Dosage Form: Powder

Patient Population: Patients requiring surgical dental procedures, expected to produce moderate post operative pain

Structure: balanced, parallel groups

Multicenter:	Yes
Blinding:	Yes
Patient Assignment Method:	randomized
Estimated Sample Size *:	220 evaluable subjects per active treatment cell 110 evaluable subjects in the placebo cell
Efficacy Variables **:	Onset of relief Duration of relief Pain Relief (PR) Pain Intensity Difference (PID) Combined PR and PID
Adverse Reactions:	Volunteered and elicited

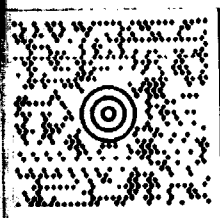
* Sample size for 80% power to detect the difference in 3 hour SPID at the $p=0.05$ level based on the following studies:

- 1) A Block Drug Company post operative dental pain study which compared 650 mg Aspirin and 195 mg Salicylamide against 650 mg Aspirin
- 2) A summary of two post-operative dental pain studies submitted by Bristol-Myers Products to FDA and obtained through FOI, which compared a combination of 500 mg Aspirin/500 mg APAP/130 mg Caffeine against 1000 mg Aspirin, using 450 subjects per treatment.

** Further description is found in Guideline for the Clinical Evaluation of Analgesic Drugs, FDA, Revised 1992

BLOCK DRUGS
(201) 434-3000
257 CORNELISON ST.
JERSEY CITY NJ 07302-3113

SHIP SEE ATTACHED
TO: XXXXXXXXXXXXXXXXXXXX
XXXXXXXXXXXXXXXXXXXX
ADDRESS LABEL
ROCKVILLE MD 20857



MD 2079-06



UPS 2ND DAY AIR 2
TRACKING #: 1Z 087 879 02 4230 3151



PKG REF 1:82920

R.K. Bourne



BLOCK DRUG COMPANY, INC.

257 CORNELISON AVENUE, JERSEY CITY, N.J. 07302-3198

TO: FOOD & DRUG ADMINISTRATION
DOCKETS MANAGEMENT BRANCH
(HFA-305)
5630 FISHERS LN, RM 1061
ROCKVILLE MD 20857

PRQ 7 6 2502 E2543

ez is training for an opportunity to represent the United States at the 2000 Olympic Games in Sydney, Australia. He has been training for the past two years in Chicago, Illinois, and currently serves as a training supervisor in the human resources department. He is a member of the global UPS Athlete Training Assistance Program (ATAP), which provides employee-athletes with the support they need to pursue their Olympic dreams.